Screening for Diabetic Retinopathy: the Utility of Nonmydriatic Retinal Photography in Egyptian Adults

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Although regular screening for diabetic retinopathy with ophthalmoscopy or retinal photography is widely recommended in the United States and Europe, few reports of its use in developing countries are available. We compared the performance of screening by retinal photography with that of indirect ophthalmoscopy by using data from a population-based survey of diabetes and its complications in Egypt. During that project, 427 persons with diabetes underwent an eye examination and fundus photography with a non-mydriatic camera through a dilated pupil. Data from the examinations of the right eye of each patient are presented. Ninety-two (22 %) of the 427 retinal photographs were ungradable; in 58 eyes (63 %), this was due to media opacity (42 eyes with cataract, 3 with corneal opacity, and 13 with both). Agreement between retinal photography and indirect ophthalmoscopy was poor (kappa = 0.33; 95 % CI = 0.27–0.39) and primarily due to the large number of eyes ($n = 79$) with ungradable photographs that could be graded by ophthalmoscopy. None of these eyes was judged by ophthalmoscopy to have sight-threatening retinopathy. Fifty-four photographs were diagnosed with greater retinopathy than found on ophthalmoscopy. Retinal photography with the nonmydriatic camera through a dilated pupil is a useful method to screen for diabetic retinopathy in most adults in Egypt. However, such screening strategies have limited use in older persons and in persons with corneal disease or cataract. © 1998 John Wiley & Sons, Ltd.

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Introduction

Diabetes mellitus is the leading cause of blindness in adults of working age in the United States of America.[1] However, much of this visual loss is preventable. Early detection of diabetic retinopathy (DR) and timely intervention by laser photocoagulation can reduce the incidence of severe visual loss by an estimated 50–60 % in people with macular oedema and by 90 % in people with proliferative retinopathy,[2] and is estimated to be highly cost-effective.[3,4]

In the United States and Europe, several organizations (American College of Physicians, American Diabetes Association, American Academy of Ophthalmology, American Optometric Association, and Retinopathy Working Party of Europe) recommend regular ophthalmoscopic screening of people with diabetes for sight-threatening DR.[5–7] Screening by retinal photography with the nonmydriatic camera through dilated pupils has been shown in many studies to perform as well as or better than ophthalmoscopy.[8–15] The utility of screening by retinal photography in developing countries has not been studied systematically.[16,17] In such countries, rates of corneal opacity and cataract, which can interfere with visualization of the retina, are typically higher.[18–20] The purpose of this study was to determine the utility of dilated retinal photography with the nonmydriatic camera for detecting DR in Egyptian adults, compare the performance of this method with ophthalmoscopy, and describe the factors associated with failure of the newer screening method.

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Patients and Methods

The data for this analysis came from a population-based survey of diabetes and its complications in Egypt (the Diabetes in Egypt Project) conducted between 1991 and 1994 by the Diabetes Institute and Central Health Laboratories, Cairo, with technical assistance from the Epidemiology and Statistics Branch, Division of Diabetes Translation, and the Environmental Health Laboratory, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. The survey provided information on the prevalence of diabetes and diabetes complications in a probability sample of the adult population.[21] Diabetes was diagnosed according to WHO criteria.[22] A total of 456 participants with diabetes were identified and underwent eye examination by three resident ophthalmologists from the Cairo Institute who had been trained by American ophthalmologists in the operation of the nonmydriatic camera. The examination included best corrected visual acuity in each eye; slit lamp examination; applanation tonometry; pupil dilation; binocular indirect ophthalmoscopy (BIO), with the right eye examined first. The same ophthalmologists performed nonstereoscopic fundus photography (one view per eye, right eye first) using a nonmydriatic 45-degree camera (Canon Retinal Camera CR4-45NM, Canon, Inc., Tokyo, Japan). Photographs were centred slightly above a horizontal line between the centre of the disk and the fovea. All photographs were graded by the University of Wisconsin Fundus Photograph Reading Center.

Grading the retinal photographs involved concurrent examination of both right- and left-eye photos (right-eye photo first) by examiners who were unaware of the patient's diabetes status and ophthalmologic examination results. The grader was asked to determine the focus of the photographs, the field definition, and the appearance of artifacts before determining the retinopathy level. The grading system for classifying DR was based on a modification of the Airlie House Classification Scheme.[23] Early nonproliferative retinopathy was defined by the presence of any microaneurysms, haemorrhages, hard exudates or small venous loops. Moderate to severe nonproliferative retinopathy was defined by the presence of soft exudates, intraretinal microvascular abnormalities or venous beading. Proliferative retinopathy was defined as fibrous proliferation or new vessels of any extent or preretinal or vitreous haemorrhage.

For comparisons of grading by the two methods (nonmydriatic camera retinal photography and BIO), four categories were used: no retinopathy, non-sight-threatening retinopathy (including pre-proliferative), sight-threatening retinopathy (exudative maculopathy or proliferative retinopathy), and ungradable retinopathy. These categories corresponded to the University of Wisconsin's photographic grading levels 10–19, 20–59, 60–80, and <10/>80, respectively.

Statistical Analysis

Analyses of right and left eyes produced similar results. Results from the right eye only are presented to avoid the problem of statistical correlation between eyes that would arise if results from both eyes were analysed together; it also eliminates possible bias in the grading of the retinopathy in the second eye.

All univariate and multivariable analyses were performed using Statistical Analysis System (SAS) software.[24] The relation between a gradable fundus photograph and a number of predictor variables (age at time of study, age at time of diabetes diagnosis, sex, duration of diabetes, glycosylated haemoglobin level, body mass index, best corrected visual acuity, presence of any cataract, presence of any corneal opacity, and intraocular pressure) was examined by univariate analysis; those variables showing a statistically significant association with the outcome variables in the univariate analysis were entered into a multiple logistic regression model with assessment of interaction terms.

To evaluate the degree of agreement between the two methods of screening, the kappa statistic was computed to take into consideration the possibility of chance agreement. For most purposes, values greater than 0.75 represent excellent agreement beyond chance, values below 0.40 represent poor agreement beyond chance, and values between 0.40 and 0.75 represent fair to good agreement beyond chance.[25]

Results

The mean age of the 456 participants with diabetes was 53.7 (range 20–85) years; 297 (65 %) were female; and 274 (60 %) had a body mass index $\geq$30 kg m^{-2}, which is equivalent to a relative weight of 140 % or greater of ideal body weight. Of the 456, 347 (76 %) had previously diagnosed diabetes and 109 (24 %) had diabetes diagnosed during the survey. Of those with previously diagnosed diabetes, most (88 %) were age 30 or older at diagnosis, and had had diabetes for a mean of 11.2 years. Two hundred and sixty-four (76 %) were being treated with oral agents only; 132 (38 %) had an HbA_1c level $\geq$10 %.

Twenty-nine (6.4 %) participants did not have ophthalmoscopy or retinal photography either because they refused to participate or because they misunderstood instructions at the time of the examination (and left before the examination was completed). The demographic characteristics of these 29 persons were similar to those of the study population; however, 62 % of the unscreened group were legally blind (defined by WHO as best corrected visual acuity less than 6/60) compared with only 7.3 % of participants who were examined.

The final group, therefore, comprised 427 participants: 417 who had both retinal photography and BIO and an additional 10 who had BIO only because their corneal opacity was judged too dense for fundus photography

(classified as having 'eyes with ungradable photos'). Of the 427 persons, 31 (7.3 %) were legally blind; 239 (56 %) had a best corrected visual acuity from 6/12 (20/40) to 6/60 (20/200), inclusive. Media opacities were detected in 151 (35 %) right eyes: 123 had cataract alone, 11 had corneal opacity alone, and 17 had both cataract and corneal opacity.

Retinal Photography

Of the 427 photographs, 92 (22 %) were described as ungradable in whole or part. In 58 eyes, this situation was due to media opacity (42 with cataract, 3 with corneal opacity, and 13 with both). In only 5 of these eyes was the opacity sufficiently dense or located such as to interfere with ophthalmoscopy. In 34 eyes, the cause of ungradability was poor focus in 25 eyes and unknown for the remaining 9 eyes.

Table 1 compares the distribution of predictor variables in eyes with and without ungradable fundus photographs. In univariate analyses, statistically significant factors associated with ungradability were as follows: age ≥60 years; presence of cataract; presence of corneal opacity; visual acuity ≥6/12. In a multiple logistic regression model, the same four variables were independently and statistically significantly associated with an ungradable photograph.

Retinal photography detected sight-threatening retinopathy in 17 (4 %) eyes: 14 eyes had exudative maculopathy based on hard exudates, 2 had proliferative diabetic retinopathy (PDR), and 1 had both conditions. Eighty-nine (21 %) eyes had non-sight-threatening retinopathy, and 229 (54 %) eyes had no retinopathy.

Table 1. Distribution of predictor variables for persons with and without gradable fundus photographs, Egypt, 1991–94 ($n = 427$ right eyes)

Predictor variable	Number of gradable photos (%)	Number of ungradable photos (%)	Prevalence odds ratio (95 % CI)
Age			
<60 yr	246 (86)	39 (14)	3.8
≥60 yr	89 (63)	53 (37)	(2.4–6.0)
Age at diagnosis of diabetes			
<30 yr	43 (84)	8 (16)	1.5
≥30 yr	292 (78)	84 (22)	(0.7–3.4)
Duration of diabetes			
<10 yr	132 (81)	31 (19)	1.3
≥10 yr	122 (76)	38 (24)	(0.8–2.3)
Corneal opacity			
no	327 (82)	73 (18)	8.5
yes	10 (34)	19 (66)	(4.2–17.1)
Cataract			
no	243 (90)	28 (10)	6.0
yes	83 (59)	57 (41)	(3.7–9.7)
Visual acuity			
6/6–6.9	145 (93)	11 (7)	5.7
≥ 6/12	186 (70)	80 (30)	(3.1–10.5)

Indirect Ophthalmoscopy

In 23 eyes, the examiners were not able to visualize the retina by ophthalmoscopy. The most common cause of poor visualization was again media opacity, found in 12 eyes: 8 with cataract, 2 with corneal opacity, and 2 with both. No information was available on the remaining 11 eyes; a possible cause of poor visualization of the retina in these cases is incomplete pupil dilation.

Ophthalmoscopy detected 5 (1 %) eyes with sight-threatening retinopathy (all with exudative maculopathy), 77 (18 %) with non-sight-threatening retinopathy, and 322 (75 %) with no retinopathy. No eyes with PDR were detected by indirect ophthalmoscopy.

Agreement Between Methods

Agreement between retinal photography and indirect ophthalmoscopy (Table 2) was poor (kappa = 0.33; 95 % CI = 0.27–0.39), primarily because of the large number of eyes ($n = 79$) with ungradable photographs that could be graded by ophthalmoscopy. However, none of these eyes was judged by ophthalmoscopy to have sight-threatening retinopathy. Agreement improves if ungraded eyes are excluded (kappa = 0.51; 95 % CI = 0.42–0.60). Compared with retinal photography, ophthalmoscopy tended to underestimate the severity of retinopathy. Forty eyes judged to have no retinopathy by indirect ophthalmoscopy were thought to have non-sight-threatening retinopathy on photography, and 12 eyes judged to have non-sight-threatening retinopathy by indirect ophthalmoscopy were thought to have sight-threatening retinopathy on photography.

Discussion

Large-scale screening for sight-threatening diabetic retinopathy requires a method that is quick, easy to use, safe, accurate, reliable, and inexpensive. Probably no single method is optimal for all situations. Retinal photography with the nonmydriatic camera has been recommended for use in the developing world or in rural areas where access to diabetes specialists or ophthalmologists is limited. In some cases, the nonmydriatic camera can be adapted for use in a mobile unit.[9,14,26,27] In countries similar to Egypt, where diabetes is rapidly becoming a major public health problem, the nonmydriatic camera might be an ideal screening tool. In our study, the camera proved to be reliable for field use and had few breakdowns and little downtime. However, the high proportion of ungradable photographs indicates a role for indirect ophthalmoscopy in some cases.

Generally, failure to obtain good quality retinal photo-

Table 2. Comparison of nonmydriatic camera fundus photography with indirect ophthalmoscopy, Egypt, 1991–94 ($n = 427$ right eyes)

Indirect ophthalmoscopy findings	Nonmydriatic camera findings				
	No retinopathy	Non-sight-threatening retinopathy	Sight-threatening retinopathy	Ungradable fundus	Total
No retinopathy	210	40	2	70	322
Non-sight-threatening retinopathy	11	45	12	9	77
Sight-threatening retinopathy	0	2	3	0	5
Ungradable fundus	8	2	0	13	23
Total	229	89	17	92	427

Kappa = 0.33 (95 % CI 0.27–0.39).

graphs occurs for three reasons: unco-operative patients, technical or camera problems, and ocular problems (e.g. corneal opacity, cataract, and vitreous haemorrhage). Technical improvements to the camera and dilation of the pupil before photography have reduced the rate of ungradable photographs.[9,15,26,28–31] A small number of screening failures caused by lack of patient co-operation, poor fixation, inaccurate focusing, media opacities or failure of mydriasis are probably inevitable; a failure rate of 5–10 % may be acceptable in a large-scale screening programme, provided that follow-up is arranged for persons with ungradable photos. The failure rate of 22 % for dilated photography found in our study suggests that a screening strategy using the nonmydriatic camera needs to be supplemented by another screeening method, such as indirect ophthalmoscopy.

The purpose of this study was not to determine the effeectiveness of a combination of screening methods. However, these findings suggest that one strategy may be to screen all persons with diabetes with the nonmydriatic camera and then to use BIO to examine all persons with ungradable photos. On its own, BIO is not recommended as a screening tool for DR because of the possibility of missing milder degrees of retinopathy and even early new vessels, but it is probably the best method for visualizing the retina through media opacities. Of 92 eyes with ungradable photos in our study, all but 13 were gradable by BIO, which graded most of these as early nonproliferative DR, and none as sight-threatening retinopathy. Even with its less-than-perfect sensitivity, a BIO exam could screen out persons with ungradable photos who do not require further referral, thereby reducing the number of false positives (ungradable photos) referred for further assessment. In our study, nonmydriatic camera screening alone would have resulted in the referral of 109 persons, 17 with sight-threatening retinopathy and 92 with ungradable photos for further evaluation. Although screening with the nonmydriatic camera plus BIO screening of the ungradable eyes has the disadvantage of requiring an ophthalmologist skilled in BIO to be present at the screening, using this strategy would have reduced the number of referrals to 30 (17 plus 13), and made for more efficient use of ophthalmologists' time.

The major limitation of this study was that lack of a gold-standard reference made it impossible to know how many eyes with true sight-threatening retinopathy and macular oedema were missed. Ideally, different screening strategies need to be compared with the gold standard of 7-field stereo retinal photography or slit-lamp biomicroscopy, to allow sensitivity and specificity to be calculated. Nevertheless, this study provides very useful comparisons on the performance of these two methods.

In summary, retinal photography with the nonmydriatic camera through a dilated pupil is a useful method to screen for diabetic retinopathy in most adults with diabetes in Egypt. However, screening strategies that use this method alone are of limited use in older persons and in persons with corneal disease or cataract. In these situations, further evaluation by ophthalmoscopy is required. Further work is needed to better determine how large-scale screening for DR with the nonmydriatic camera will perform in this setting.

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